

Amendments to the Specification:

On page 22, please replace the paragraph starting at line 5 with the following amended paragraph:

To produce a hypoxically regulatable retroviral construct long a terminal repeat (LTR) plasmid was generated from the retroviral plasmid pLNSX (Miller and Rosman 1989 Biotechniques 7 980-990) by cutting at the NheI sites within the LTR, removing the majority of the intervening retroviral genome sequences and religating the backbone. This produces an LTR plasmid in which enhancer and enhancer/promoter swaps can be engineered. The retroviral enhancer was exchanged with the PGK hypoxia response element (HRE) by performing an NheI/XbaI swap. The resultant vector was then recut with NheI and the Nhe I fragment of the retroviral genome designated MOI was inserted. MOI was generated from the MFG vector (Bándara et al 1993 PNAS 90 10764-10768) by the generation of a minimal functional packaging signal using PCR with the following primers:

HindIIIIR: GCATTAAAGCTTTTGCTCT (SEQ ID NO:1)

L523: GCCTCGAGCAAAAATTCAGACGGA (SEQ ID NO:2)

Please replace the paragraph bridging pages 25-26 with the following amended paragraph:

Sequences from a region approx. 300-375 bp upstream of the transcription start of the human Enolase A gene were chosen containing three HIF-1 consensus binding sites (Semenza et al 1996 J. Biol. Chem. 271: 32529-32537. The following oligonucleotides were synthesised to assemble this sequence and add a BglII site at the 5' end and a BamHI site at the 3' end.

Lead strand (75-mer)

GATCTGAGGGCCGGACGTGGGGCCCCAGAGCGACGCTGAGTGCGTG
CGGGACTCGGAGTACGTGACGGAGCC
CCG (SEQ ID NO:3)

Complementary strand (75-mer)

GATCCGGGGCTCCGTCACGTACTCCGAGTCCCGCACGCACTCAGCGT
CGCTCTGGGGCCCCACGTCCGGCCCC
TCA (SEQ ID NO:4)

Please replace the paragraph bridging pages 26-27 with the following amended paragraph:

Similarly, oligonucleotides were synthesised representing the HRE from the murine LDH gene (Firth et al 1995 J. Biol. Chem. 270: 21021-21027. The sequence chosen lies 15bp upstream of the LDH TATAA box. It contains a HIF- 1 consensus binding site and a putative cyclic AMP-response element. This HRE was also introduced at the BglIII site of pGL3 -pro.

Lead strand (56-mer)

GATCTCTACACGTGGGTTCCCGCACGTCCGCTGGGCTCCCACTCTGA
CGTCAGCGG (SEQ ID NO:5)

Complementary strand (56-mer)

GATCCCGCTGACGTCAGAGTGGGAGCCCAGCGGACGTGCGGGAACC
CACGTGTAGA (SEQ ID NO:6)